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ABSTRACT

The introductory discussion focuses on the change in the current scientific climate regarding the role of heredity in the etiology of behavioral disorders. The author and his colleagues embarked on a series of studies, using naturally occurring adoptions as their subject source, to tease apart hereditary and environmental factors thought to be implicated in schizophrenia. The bulk of the paper is an elaboration of eight adoption strategy research designs which they have developed. These designs focus variously on the adoptees, their natural families and adoptive families, in an effort t collect data which might clarify the relative contributions of heredity and environment, as well as heredity environment interaction. Where currently available, data is presented and tentative conclusions drawn. The author closes with an optimistic prediction that in the next decade there will be a marked acceleration in the acculumation of knowledge about the hereditary and environmental factors involved in the etiology of behavioral disorders. (TL)

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The Design of Studies to Evaluate Hereditary and Environmental Contributions to the Etiology of Behavioral Disorders*

David Rosenthal**

For good and various reasons, though not compelling ones, American psychologists have long shown a remarkable indifference to the possible role of heredity in the etiology of behavioral disorders. I will not try to document this statement here, but I will take just a little time from my presentation to mention some of the reasons for this indifference or, if you will, this avoidance behavior.

One reason clearly had to do with a healthy skepticism regarding the validity and reliability of assessing traditionally defined diagnostic categories, such as schizophrenia, manic-depressive psychosis, psychoneurosis, psychopathy, alcoholism, homosexuality, and others. Another reason was the association of fallacious, malevolent hereditary "theories" with the monstrous ideology of the Nazi Herrnvolk and their dehumanized, genocidal slaughtering of innocents. Also, even today, "genetic" research has sometimes been linked to racism and suppression of black people. A third reason was the cherished American concept of personal freedom: any theory that implied a genetic determination of behavior, even in part, was inherently repugnant to Americans in that it threatened to delimit our concept of personal freedom as well as our subjective or collective consciousness of such freedom; to accept such a limitation was virtually unthinkable. A fourth reason had to do with the fact that so-called

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genetic research has often been cavalier in its disregard of basic, accepted methodological practices, such as the use of a control group, or making assessments while blind with respect to the relationship between a subject and the index case in a given study. Thus, many sophisticated psychologists rejected the entire literature on this subject out of hand and refused to school themselves in the principles and methods of human genetics that might have permitted them to assess for themselves the possible role of hereditary factors in the behavioral disorders. A fifth reason reflected a popular but mistaken belief that if a disorder had a genetic basis, it was ipso facto untreatable; a concept of therapeutic nihilism, even though unjustified, was not one that Americans would tolerate very long. A sixth reason was that psychologists were too absorbed in psychodynamic explanations of psychopathology and in principles of learning to find any room for an ego-alien notion such as genetics in their conceptualization of behavioral disorder. And a seventh reason was that none of the behavioral disorders followed any clear Mendelian distribution, a fact that generated skepticism about the relevance of genetics in this realm of study.

Today our cultural climate may be as wary as ever with respect to any implied association between heredity and behavior. However, our scientific climate in this regard has begun to change appreciably, probably abetted by the formulation of the Watson-Crick model for DNA and the subsequent excitement in the development of molecular genetics, by the relative disenchantment with various aspects of learning theory, and by the growing dissatisfaction with the limited results of psychodynamically

oriented therapies. Also, during the past fifty years, evidence for an hereditary contribution to the psychopathologies had been gathering steadily in Europe, and to a lesser extent in the United States. The evidence might have been fallible because of methodological insufficiencies, but its accumulating weight began to demand attention here.

What was the nature of this evidence? It was based essentially on two kinds of studies.

1. Consanguinity studies. Here the assumption was that if a disorder occurred more frequently in the relatives of an affected individual than in the population at large, this finding provided evidence for an hereditary contribution to that disorder. Moreover, if the frequency of the disorder was greater in first degree relatives as compared to second or third degree relatives, this finding reinforced the evidence for an hereditary contribution. However, investigators who made these assumptions were ignoring the possibility that nongenetic factors could also have accounted for such distributions of the disorder. Such nongenetic factors could be psychological, such as parental behavior that has been described as attention-fragmenting, chaotic, or double-binding, to name a few of the terms used by psychodynamic environmentalists, or these factors could be sociocultural, so that a trait such as poverty might show the same patterns of correlation between degree of consanguinity and degree of poverty that one might find with various forms of psychopathology.

2. Twin studies. The classical twin study design is based on the fact that monozygotic twins have exactly the same heredity whereas dizygotic twins have only about half their genes in common. Therefore

it has been assumed that if pairs of monozygotic twins are concordant, i.e., have the same psychopathology, more often than pairs of dizygotic twins, then such a finding constitutes evidence of a genetic contribution to the disorder. This inference is based on the assumption that intrapair environmental factors are the same for both monozygotic and dizygotic twins. Usually the environmental factors that have been considered most relevant involved a common rearing in the same home. Since both members of the monozygotic and the dizygotic pairs were reared together, then the assumption of equal intrapair environmental variance across groups was considered to have been met.

However, psychological factors unique to monozygotic twins, especially that of shared identity, have been described vividly by several investigators who maintain therefore that the equal environment assumption is ill-founded, that solely on psychological grounds one would predict a higher concordance rate for monozygotic twins, and that the inference of a genetic contribution to the disorder is not warranted based on such findings alone. We should note too that the classical twin study design invokes a unidirectional hypothesis; the prediction is always that there will be greater intrapair similarity for monozygotic twins. But there is almost never any reason to predict greater intrapair similarity for dizygotic twins, whether for genetic or environmental reasons. Therefore, the traditional twin studies of psychopathology have been suggestive but not conclusive. Studies of twins reared apart could be helpful in that the problems associated with shared identity cannot arise in separated twins. However, it is difficult to obtain representative samples of separated twins, and the happenstance case by case reporting of such twins might involve selective bias.

For these reasons, Dr. Seymour Kety and I began a series of conversations about ten years ago in which we decided to embark on a different research strategy in attempting to resolve the old controversies. We planned to use naturally occurring adoptions to tease apart the hereditary and environmental factors that were thought to be implicated in most forms of psychopathology. Not long afterward we were joined by Dr. Paul Wender who had had the same idea. The psychopathology that we chose to work on was the one called schizophrenia. Most of the previous genetic research by far had been devoted to this disorder, and it was th one of greatest concern to the mental health professions and to the population at large. The environmental variable we chose to work on involved type of rearing, which many psychiatrists, psychologists and laymen felt was the primary etiologic agent in the schizophrenic disorders. Since rearing involves a huge subset of variables, we chose to focus more specifically on rearing by or with a schizophrenic relative.

Of course, the idea of using adoption to separate the genetic and rearing variables is not new. Psychologists have employed this research strategy liberally in the study of intelligence (Burks 1928, Honzik 1957, Skeels 1936, Skodak 1939, Skodak and Skeels 1949). One adoption study has been carried out with respect to alcoholism (Roe, 1945) and one with respect to antisocial behavior (zur Nieden, 1951). Yet, considering the potential value of such research, the adoption strategy has been used very sparsely. There were good reasons for this apparent neglect. Adoption agencies and the courts have been zealous in their desire to protect all parties to the adoption, the biological parents, the adopting parents and the child, and the agencies have usually been

unwilling to divulge any information about them to outsiders. Without the agencies' cooperation, it becomes extremely difficult to mount any adoption study at all, although we have generated one research strategy that circumvents this problem. Nevertheless, to carry out our studies in the way we wanted, we eventually felt obliged to go abroad, where cooperation was possible. Perhaps in the future there will be some liberalization of American agencies' rules with respect to information released to researchers. The researchers in turn will have to commit themselves to prescribed practices and constraints that must be acceptable to the agencies.

Although the adoption strategy is not new, Dr. Kety, Dr. Wender and I have developed research designs that build upon and amplify the potential usefulness of this strategy. We did not have all these designs in mind when we started, but as happens often in research, once we were enmeshed in the work itself, new findings and problems that arose suggested new methodological approaches. In this presentation, I will focus on these research designs rather than on the details of our research findings. However, I will touch briefly upon the findings, when they are available, using them primarily to indicate the power of the designs and the nature of the information they yield. Through all these designs, we treat heredity as though it were an independent variable, just like any other independent variable in a well carried out laboratory experiment.

The first group of studies that I will talk about has been carried out in Denmark, under the excellent supervision of Dr. Fini Schulsinger.

In the first of these studies, (Kety et al., 1968) we were interested in the incidence of schizophrenic disorders in the biological and adoptive relatives of schizophrenics and nonschizophrenics, respectively. The design of the study is shown in Figure 1.

Place Figure 1 about here.

Because the focus of the study is the relatives of the adoptees rather than the adoptees themselves, we may call it the Adoptees' Families Design. In this study we are testing two opposed hypotheses. 1. If schizophrenic disorders are heritable, we should find a higher prevalence of such disorders among the biological relatives of our schizoprhenic index cases than among the biological relatives of the matched controls. 2. If schizophrenic disorders are transmitted behaviorally, and at least in good part by rearing parents whose own behavior is confused, disorganized, erratic or chaotic, to mention some of the terms cited in the literature, we should expect that the index cases would have a greater number of adoptive relatives with schizophrenic disorders than would be found in the adoptive relatives of the controls.

To carry out this design, we began by collecting identifying information on all persons who had formally been given up for non-family adoption at an early age in the greater Copenhagen area between 1923 and 1947. There were almost 5,500 such adoptions. From the records we learned the name and birthdate of the adoptee, and the names and other identifying information of the adopting and biological parents. From

the Psychiatric Register, we found out which of the approximately 5,500 adoptees had been admitted to a psychiatric facility. The hospital records for each admitted adoptee were examined by two Danish psychiatrists, and the main information provided by one psychiatrist was sent to the American investigators. All five made their own independent diagnoses. By this procedure, we were able to select 33 index cases. Of these, 16 were chronic or process schizophrenics; 7 were acute schizophrenic reactions of the schizophreniform, schizo-affective or paranoid type; and 10 were cases of borderline schizophrenia.

We selected from among the remaining adoptees in the total pool a control group who did not have a file in the Psychiatric Register and who were matched individually to the index cases with respect to sex, age, pretransfer history, and socioeconomic status of the rearing family.

In determining the rates of schizophrenic disorders among the relatives of our 66 probands, we did not examine the relatives personally. Instead, we first identified each biological or adoptive relative who was either a parent, sib or half-sib of a proband, and we then identified each one of these relatives who had a known psychiatric history. These histories were abstracted from records by a Danish psychiatrist who did not know if the individual case he was abstracting was the biological or adoptive relative of an index case or a control. The psychiatric abstract was then sent to the U. S. investigators who independently made their own diagnoses while they were similarly blind regarding the relationship of the relative to the proband. Diagnostic differences among the four major investigators were settled by discussions based on more complete data from the records, before we broke the relationship code.

At this point, I would like to call to your attention two important features of our research. The first is that, wherever possible, we keep all examiners blind with respect to the index or control status of the subject under examination. We are almost always successful in this respect. This procedure insures against the possibility of bias either for or against any preferred hypothesis that the examiner may hold. The second feature has to do with the fact that we have included a broad spectrum of disorders in the ones I am calling schizophrenic. These include not only the classical chronic, process types of cases, but patients called doubtful schizophrenic, reactive, schizoaffective, borderline or pseudo-neurotic schizophrenic, or schizoid or paranoid. If we dealt only with hardcore schizophrenia, our n's would be too small to make any of these studies meaningful. However, a more positive reason for including the spectrum of disorders is that in the process, we hope to be able to determine whether any or all of these disorders, which phenotypically have strong resemblances to hardcore schizophrenia, are genetically related to it as well. (For a more complete discussion of this issue, see Rosenthal, 1970.)

With respect to Figure 1, the major finding was that we obtained the highest concentration of schizophrenic spectrum disorders among the biological relatives of the schizophrenic index cases. The rates for such disorders did not differ appreciably in the other three cells. Thus, this finding provides strong evidence for an hereditary contribution to such disorders. However. I want to point out that Figure 1 does not comprise a true fourfold table. That is why a double line is drawn to

separate the biological and adoptive halves. The reasons for this are practical rather than theoretical. I will mention only the major reason. It is important to understand that both the adopting and biological parents of our adoptees represent screened populations. The screening with respect to adopting parents is well-known, since adoption agencies have long taken the view that mentally ill people do not make the kinds of parents that serve the best interests of the child. But biological parents are also screened in that if they are known to be schizophrenic, adoption agencies may be reluctant to place their children for formal adoption. Instead the children may be reared in foster homes or in institutions. Moreover, at least in Denmark, schizophrenic women, or women with schizophrenia in their families, may request and have legal abortions. Thus, such children are never even born and cannot come into the pool of probands in Figure 1. We do not know the extent of screening in the biological and adopting families, but the screening may be unequal. This fact limits the possible range of differences that might otherwise be found in this type of study, but it does not invalidate the procedure. It also means that we can compare the two groups of biological relatives, and the two groups of adoptive relatives, but we cannot now make valid comparisons between biological and adoptive relatives.

The second model (Rosenthal et al., 1968) is shown in Figure 2.

Place Figure 2 about here.

We call it the Adoptees' Study Design because the focus of study is the adoptees themselves rather than their relatives. The design asks the

question: What is the fate of offspring of schizophrenic parents when these offspring are reared adoptively? In this study, the starting point is the approximately 10,000 biological parents of our pool of adoptees. A search was conducted to see who among these parents had a file in the Psychiatric Register. The hospital records of each such parent were reviewed in detail by a psychiatrist who completed a prescribed form which was reviewed independently by the American investigators. If we agreed that the parent's diagnosis belonged in our spectrum of schizophrenic disorders, or was a clearcut or possible case of manic-depressive psychosis, the adopted-away child of that parent was chosen as an index case. From among the remaining adoptees, we chose as controls those whose both biological parents had no known psychiatric history; i.e., neither parent had a file in the Psychiatric Register. Controls were matched to the index cases for sex, age, age at transfer to the adopting family, and the socioeconomic status of the adopting family.

The index and control subjects were invited to participate in a study of the relationship between environment and health. We were able to achieve almost 80 percent cooperation, an acceptable figure, and the two groups did not differ in this respect. At this time, we are able to report on 76 index cases and 67 controls. The subjects were given a semi-structured psychiatric interview by Dr. Joseph Welner that lasted from about 3 to 5 hours. Each subject also had one and a half days of psychological testing, but we will not be able to present the test findings now. The examinations of all subjects spanned a period of four years.

The main finding of this study is that there is a significantly

greater number of schizophrenic spectrum disorders among the index cases than among the controls. Three cases were called clearcut schizophrenia by Dr. Welner. All three were index cases. However, only one of these had been hospitalized for the disorder. As a matter of fact, the rate for hospitalized schizophrenia and for diagnosed schizophrenia tends to be appreciably lower than the rates usually found in Scandinavia for the nonadopted offspring of schizophrenics. Therefore, this study leads us to the twofold conclusion that heredity is contributing significantly to the development of schizophrenic spectrum disorder, and that adoptive rearing contributes to the reduced expressivity of such disorder. In both studies presented, evidence is accumulating that the disorders in our spectrum are genetically related, with the probable exception of reactive schizophrenia, which may have to be excluded from the spectrum.

Now I would like to show you a research model that is based on an experimental design that has been used in the past by behavioral geneticists: (Ginsburg and Allee 1942, Fredericson 1952, Broadhurst 1961, and Ressler 1963). It has generally been referred to as a cross-fostering or reciprocal fostering model. To review briefly the essentials of this model, let us assume that the experimenter is interested in learning whether he can breed in a trait such as social dominance. He would first decide on a test or criterion for the trait. He would then run his starting pool of animals through this test and separate those who test high (called dominant) and those who test low (called submissive). He would then inbreed the dominant animals and inbreed the submissive animals, and repeat the test with the next generation. This procedure is continued as long as the respective inbreedings continue to increase the test discrimination

between the dominant and submissive groups. Let us say that at the nth generation, the experimenter decides that he can no longer increase the discrimination. At this point, he needs to ask himself whether he has successfully bred in the trait or whether each generation had become more dominant or more submissive because it had in turn been reared with successively more dominant or more submissive parent populations. Therefore, he checks this possibility with the n + 1 generation. He does this by transposing the n + 1 dominant animals to be reared by submissive dams, and n + 1 submissives to be reared by dominant dams. Then he runs the n + 1 adult generation through his test to see what effect the transposed rearing may have with respect to the test performance.

Now, we cannot control human breeding, but we can follow the model somewhat by thinking of our pool of adoptees as an n + 1 generation. The design is shown in Figure 3.

Figure 3 about here.

We begin with the biological parent generation. From among them we select those who are schizophrenic and who are presumably breeding the trait. Among their adult offspring, we select those who were reared by adoptive parents who had had no schizophrenic disorder, as far as we can tell. These offspring constitute one testing group. Then we select from among those biological parents who had had no schizophrenic disorder, as far as we can tell, those whose offspring had been reared by an adopting parent who did have some schizophrenic disorder. These offspring comprise

our second testing group. The two groups of offspring are then compared with respect to the trait in question. Although we have not yet analyzed the data in this study, a preliminary look at the data suggests that the incidence of schizophrenic spectrum disorders tends to be about equal for the two cross-fostered groups. Should this tentative observation prove true, it would not mean that heredity is irrelevant, but rather that rearing by a schizophrenically disordered parent may also be influential in the development of spectrum disorders.

Although the cross-fostering design has its own built-in elegance, what it does in effect is to pit two competing hypotheses against one another. However, we also want to know in more detail the effect of each independent variable considered separately. Now that some statistical evidence is accumulating to the effect that rearing by a schizophrenic parent may itself produce spectrum disorders in offspring, it is important that we have a research model that provides a clean test of this hypothesis. This model is shown in Figure 4.

Figure 4 about here.

In this model, we begin with biological parents who do not have any schizophrenic spectrum disorder, as far as we can tell. This is done to insure to the maximal extent possible that the offspring under study are as free of genetic contamination as we can make them. Preferably, all biological parents should be examined personally and in depth to make the determination of no spectrum disorder, but we have not as yet been able to do this. Now we ask the question: when there is minimal or no genetic

predisposition in the child, will rearing by a schizophrenic parent induce spectrum disorders in the child? Thus, we have two groups of adoptees. The first or index group are reared by a schizophrenic spectrum parent, the second or control group by rearing parents who are free of spectrum disorder. The second group, which is matched to the first group for various relevant variables, constitutes as ideal a control group as we can find in that both their biological and rearing parents are free of spectrum disorders. Any psychopathology that we find in these offspring should arise from other factors. Any psychopathology in the index group in excess of that occurring in this "idealized" control group represents the contribution of rearing by a schizophrenic parent. We cannot at this time report any findings on this study, but will do so in the future.

Now, we must be alert to another alternative. It may be that rearing by a schizophrenic parent is insufficient <u>per se</u> to induce spectrum disorders in offspring, but that such rearing could raise havoc with genetically predisposed individuals. To test this possibility, we require a research model such as that shown in Figure 5.

Figure 5 about here.

This design is exactly like that of the previous design, with one important exception: this time <u>all</u> subjects must have a biological parent who has schizophrenic spectrum disorder. Thus, from a genetic standpoint, the amount of hereditary predisposition for such disorder should be the same for our two groups, and it should be considerable.

Again the difference between the groups occurs in the rearing variable. Actually, it is not possible to carry out such a design in pure form, at least not in Denmark, since this would require that both groups of subjects should be adoptees. However, the likelihood of generating a sample in which the subjects have a biological parent who is schizophrenic and are then given up for adoption to a rearing parent who is also schizophrenic is, fortunately, very small. Thus, to carry out the intent of the design, we have had to substitute for adoptees a group of subjects who had a schizophrenic parent and who were reared in the parental home at least during their first fifteen years of life. This represents the group in which the hypothesized genetic and rearing factors would be truly coacting to produce the schizophrenic phenotype. The comparison group of adoptees provides a baseline that represents only the genetic contribution, without the superimposition of rearing by a schizophrenic parent. Any difference between the two groups should represent the coaction or true interaction effect. We have collected a matched sample of nonadoptees to carry out this design, but the research material has not yet been subjected to analysis.

We are now in a position to bring together several of the samples of subjects we have collected and arrange them in a fourfold table that represents the various combinations of genetic and rearing variables, as shown in Figure 6.

Figure 6 about here.

Thus, we have two types of rearing variables, schizophrenic and

nonschizophrenic, and two types of genetic variables, schizophrenic and nonschizophrenic. Three of the four cells contain adoptees. Two diagonal cells represent subjects in the Cross-fostering design. The adoptees in the lower right cell are obtained from the control group in the Adoptees Study Design. The upper left cell, unfortunately, has to be represented by the nonadoptees obtained in the previous design, and that is why it is represented by a double line. Thus, in one cell the factor of adoption does not hold and we do not know to what extent this fact invalidates the findings of this otherwise neat design. Nevertheless, we may carry out such an analysis if we have reason to think it will be worthwhile.

The next study I want to present was carried out in Bethesda (Wender et al., 1968). It represents the kind of study that can be done without requiring the cooperation of adoption agencies. The design is based on the following rationale. Many investigators have maintained that a child develops schizophrenic disorder because his parents have subjected him to various kinds of noxious rearing. In accounting for the elevated incidence of schizophrenia among the parents of schizophrenics, they point out that such parents are more likely than normal parents to emit these noxious behaviors in regard to their children and that, therefore, the elevated incidence of schizophrenia among parents of schizophrenics is to be expected on rearing grounds alone. Alanen (1966) reported that parents of schizophrenics had a higher rate of severe psychopathology than did the parents of neurotics, and inferred that the correlation between parents and children regarding severity of psychopathology represented evidence for behavioral transmission. However, such findings could

as well imply that the elevated rates of schizophrenia and severe psychopathology in the parents represent genetic factors that are transmitted to offspring who in turn manifest schizophrenic disorder. To test these alternative hypotheses, we invoke the design shown in Figure 7.

Figure 7 about here.

In this design, we are concerned with the parents of schizophrenics. Since in the type of study done by Alanen and other investigators the genetic and rearing variables are confounded in the same parents, we again resort to adoption to separate the two variables. We begin by finding young adult schizophrenics who had been given up for adoption early in life. This can best be done by interviewing all new admissions to mental hospitals, and their parents. It is a tedious job but it is feasible. From among other schizophrenic admissions who were home reared, we find a group that is matched to the adopted schizophrenics with respect to the variables deemed most relevant. The third group in the shown design is used to control for the factor of adoption. However, this group of adoptees is free of schizophrenic disorder. The subjects studied are not the offspring, but the parents. The particular focus of the study is the adoptive parents of the schizophrenics. Our reasoning goes like this: If the schizophrenia in the children represents primarily genetic influences, the degree of psychopathology in their adoptive parents should not be severe, as Alanen had reported, and should be less than that of the biological parents of schizophrenics. If the schizophrenia in the children represents the effects of noxious behavioral influences, the degree of psychopathology among the adoptive parents should be the same as that

found in the biological parents.

Our findings indicated that the degree of psychopathology in the adoptive parents of schizophrenics was significantly less than that of the biological parents of schizophrenics but significantly greater than that of the adoptive parents of normal subjects. Thus, it is possible to have schizophrenia in offspring who are not subjected to the noxious influences associated with severe psychopathology in the rearing parents. The finding of a difference in degree of psychopathology between the adoptive parents of schizophrenics and the adoptive parents of normals could have any of several explanations which I will not take the time to discuss here. It is interesting that on a word association test, the biological parents of schizophrenics produced more unusual responses than did the adoptive parents of schizophrenics.

To carry out the last design that I shall present, I went to Israel. This study was done without the collaboration of my two brilliant colleagues, Dr. Kety and Dr. Wender. As noted earlier, our attempts to generate a clean fourfold-table design by using adoption fell short of our goals. However, we can forego the advantages conferred by adoption if we can specify two different environments that bear on the kinds of rearing we have been talking about. Israel provided two such environments, the kibbutz and the nuclear family types of rearing. The reasoning underlying the study goes like this. In the typical nuclear family, if a parent - let us say the mother - is schizophrenic, the child is likely to endure the following psychological hazards: the mother may be too autistic to attend or to be responsive to the child's needs and she may program reinforcements haphazardly and unpredictably, thus impairing the child's

cognitive training and his affective and motivational integration; during the times she is not hospitalized, she is likely to be the only person in the child's environment during most of each day, so that during the greater part of the time that he is awake, the child has no other model with whom to identify during his formative years; sometimes the parent undergoes successive hospitalizations, so that the child may suffer increased insecurity each time he loses her, and he may develop a deep sense of mistrust of the world around him; sometimes the home will be broken, the child may be reared by relatives or friends, in institutions, or he may be shuttled back and forth in various combinations of such rearing; he may be isolated from other children; if he has siblings, they are likely to be similarly influenced and they may tend to influence each other noxiously in turn.

However, although kibbutzim vary among themselves in a number of ways, in the main they may provide greater protection for the child who has a schizophrenic parent. For example, the child grows up in children's houses under the guidance of trained caretakers. During the greater part of each day, he receives the same tutelage and training as do other children. During evenings and holidays when the children and parents visit together, the child will visit with both the well parent and the sick parent, and the well parent may help to neutralize any noxious impact of the sick parent. Usually, the child is well-known to other adults in the kibbutz and they may serve as parent surrogates. If the sick parent requires hospitalization, the child suffers minimal disruption of his life. He remains in the same children's house with the same caretakers,

teachers and friends. He lives in the same community, and he can still visit with the well parent during the evenings and holidays.

The design for this study is shown in Figure 8.

Figure 8 about here.

This study was carried out under the supervision of Dr. Shmuel Nagler and Dr. Sol Kugelmass. The key cell is in the upper lefthand corner. We had to find children who were born and reared in a kibbutz and who had a schizophrenic parent. We were able to find 25 such cases. We then found 25 matched cases who lived in the usual nuclear family situation and who also had a schizophrenic parent. For kibbutz controls, we selected a group of children who were reared in the same children's houses as the index cases, but whose parents had no spectrum disorder, and for nuclear family controls we selected children from the same neighborhood and classroom, but without a schizophrenic parent. The children had two days of examination. They were brought in pairs, each index case and his control, but all examiners were kept blind as to which child was which. Thus, we had the rare opportunity to observe and test both the index and control subjects in the same situation. The children ranged in age from 8 to 14. Our major dependent variables involve the degree and type of psychopathology found in the four groups of subjects. With respect to each variable, we can apportion the amount of variance contributed by genetic background or parentage, the amount contributed by type of rearing environment, and the amount contributed by the genetic-rearing interaction. At this time, all data are being analyzed. We hope to begin reporting

our findings in the next year. It is worth noting that this is a generalized design that avoids the problems confronting us in adoption studies, and that can be applied whenever the investigator can specify two contrasting types of environment, whether they have to do with rearing or with other kinds of environmental or experiential phenomena. The latter can be conceptualized narrowly or broadly, depending on the investigator's theoretical predilection.

In closing, I would like to say that only a decade ago there existed a widespread air of pessimism about the possibility of ever unraveling the hereditary and environmental factors involved in the etiology of the behavioral disorders. Today, the outlook is completely opposite. During the seventies we should see a marked acceleration in the accumulation of knowledge in this important field.

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Probands	RELATIVES: Biological	RELATIVES: Adoptive
Schizophrenic		
Control (nonschizophrenic)		

Figure 1. Adoptees' Families Design

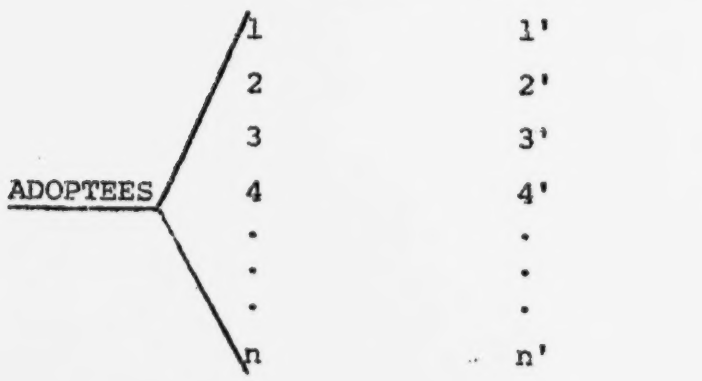

Figure 2. Adoptees Study Design

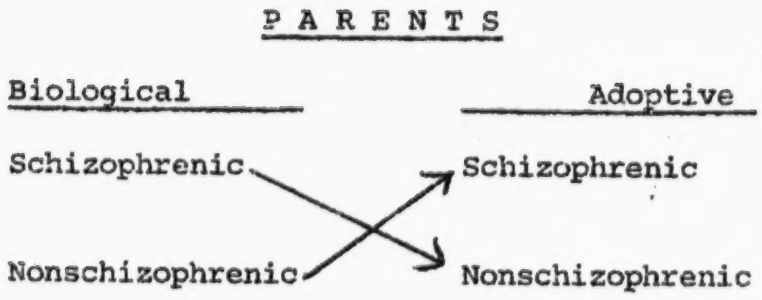

Figure 3. Cross-Fostering Design

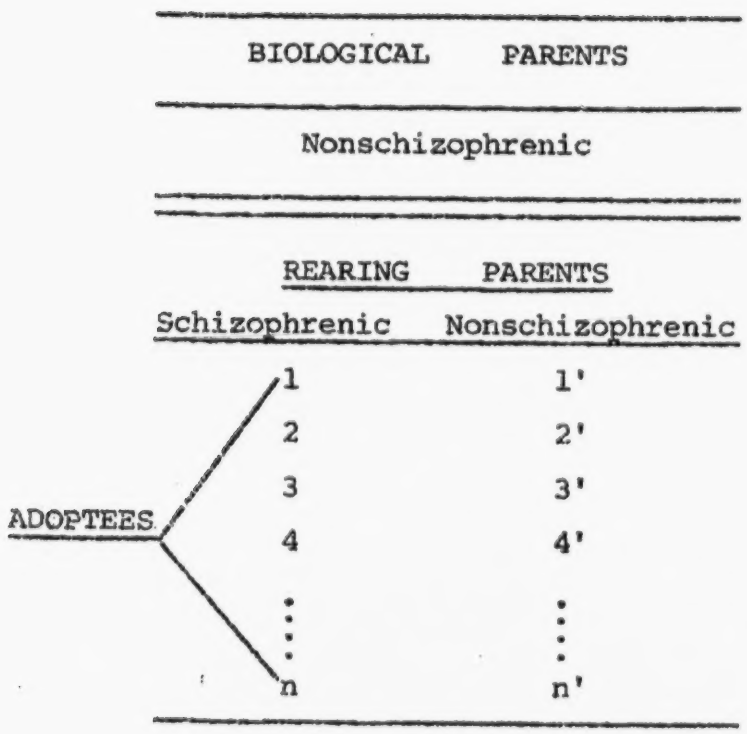

Figure 4. Design to Test the "Pure" Environmentalist Hypothesis.

	BIOLOGICAL PARENTS	
	Schizophrenic	
	REARING PARENTS	
	Schizophrenic	Nonschizophrenic
ADOPTEES	1	1'
	2	2'
	3	3'
	4	4'
	⋮	⋮
	n	n'

Figure 5. Design to Test the Effects of the Hypothesized Environmental Variable Coacting with the Genetic Variable.

GENETIC BACKGROUND	TYPE OF REARING	
	SCHIZOPHRENIC	NONSCHIZOPHRENIC
Schizophrenic	Nonadoptees	Cross Fostering
Nonschizophrenic	Cross Fostering	Controls

Figure 6. Modified Design to Test for Statistical Interaction Between the Hypothesized Genetic and Environmental Variables.

	DIAGNOSIS OF PROBANDS		
	Schizophrenic	Schizophrenic	Nonschizophrenic
REARING PARENTS	Adoptive	Biological	Adoptive

Figure 7. The Adoptive Parents Study Design

PARENTAGE	TYPE OF REARING	
	Kibbutz	Nuclear Family
Schizophrenic	25	25
Nonschizophrenic	25	25

Source	df
Parentage	1
Rearing	1
Parentage X Rearing	1
Error	96
Total	99

Figure 8. Generalized Design for Estimating the Relative Contributions of Heredity, Environment, and Heredity-Environment Interactions.